

### **Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

### **Listing of Claims:**

1. (Original) A conjugate comprising
  - a) a trifunctional cross-linking moiety, to which is coupled
  - b) an affinity ligand via a linker 1,
  - c) a cytotoxic agent, optionally via a linker 2, and
  - d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens expressed on mammalian tumour surfaces with an affinity-binding constant of at least  $5 \times 10^6 \text{ M}^{-1}$ , wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1.
2. (Original) The conjugate according to claim 1, wherein the anti Erb antibody or variants thereof are directed to Erb 1, Erb 2, Erb 3, and/or Erb 4 antigens expressed on mammalian tumour surfaces.
3. (Cancel)
4. (Currently amended) The conjugate according to claim 1 ~~any one of the preceding claims~~, wherein the anti Erb antibody is coupled to the trifunctional cross-linking moiety via a linker 3, and wherein the bond formed between linker 3 and the anti Erb antibody is either covalent or non-covalent with a binding affinity constant of at least  $5 \times 10^8 \text{ M}^{-1}$ .
5. (Currently amended) The conjugate according to claim 1 ~~any one of the preceding claims~~, wherein the cytotoxic agent is a radionuclide, chemotherapeutical agents, a synthetic or naturally occurring toxin, immunosuppressive or immuno stimulating agents, radiosensitizers, enhancers for X-ray or MRI or ultrasound, non-radioactive elements, which can be converted to radioactive

elements by means of external irradiation after the anti Erb antibody carrying said element has been accumulated to specific cells or tissues, or photoactive compounds or compounds used in photo imaging or photodynamic therapy, or any other molecule having the same or a similar effect, directly or indirectly, on cancer cells or cancer tissues.

6. (Cancel)

7. (Currently amended) The conjugate according to claim 1 ~~6~~, wherein when the cytotoxic agent is a radionuclide and is bound to the trifunctional cross-linking moiety via a cytotoxic agent binding moiety.

8. (Original) The conjugate according to claim 7, wherein the cytotoxic agent binding moiety form aryl halides and vinyl halides for radionuclides of halogens, and comprises  $N_2S_2$  and  $N_3S$  chelates for Tc and Re radionuclides, amino-carboxy derivatives, preferably EDTA, triethylenetetraaminehexaacetic acid, and DTPA or derivatives thereof, wherein the DTPA derivatives are Me-DTPA, CITC-DTPA, and cyclohexyl-DTPA, and cyclic amines, preferably NOTA, DOTA and TETA, and derivatives thereof, for In, Y, Pb, Bi, Cu, Sm and Lu radionuclides, or any other radionuclide capable of forming a complex with said chelates.

9. (Currently amended) The conjugate according to claim ~~claims~~ 7 ~~and 8~~, where in the cytotoxic agent binding moiety comprises DOTA and the cytotoxic agent is  $^{90}Y$  for therapeutic application or  $^{111}In$  for diagnostic application.

10. (Currently amended) The conjugate according to claim ~~claims~~ 6 ~~and 7~~, wherein the cytotoxic agent binding moiety comprises DOTA and the cytotoxic agent is  $^{177}Lu$  for both diagnostic and therapeutic application.

11. (Cancel)

12. (Currently amended) The conjugate according to claim 1 ~~any one of the preceding claims~~, wherein the affinity ligand is a moiety which binds specifically to avidin, streptavidin or

any other derivatives, mutants or fragments of avidin or streptavidin having essentially the same binding function to this affinity ligand.

13. (Currently amended) The conjugate according to claim 1 ~~any one of the preceding claims~~, wherein the biotin derivative is chosen from the group consisting of norbiotin, homobiotin, oxybiotin, iminobiotin, destibiotin, diaminobiotin, biotin sulfoxide, and biotin sulfone, or derivatives thereof having essentially the same binding function, preferably with an affinity-binding constant of at least  $10^9 \text{ M}^{-1}$ .

14. (Currently amended) The conjugate according to claim 1 ~~any one of the preceding claims~~, wherein the trifunctional cross-linking moiety is chosen from the group consisting of triaminobenzene, tricarboxybenzene, dicarboxyaniline and diamino benzoic acid.

15-17. (Cancel)

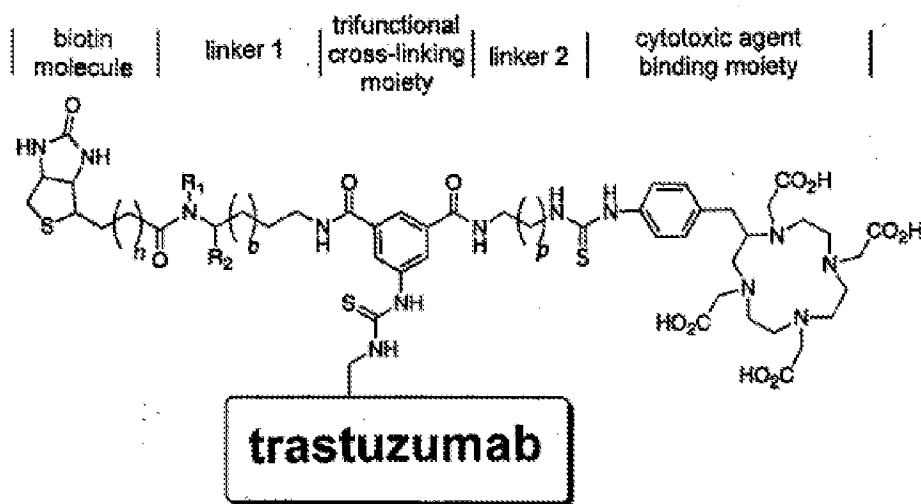
18. (Currently amended) The conjugate according to claim 1 ~~any one of the preceding claims~~, wherein linker 2 provides a spacer length of 1-25 atoms, preferably a length of 6-18 atoms.

19-20. (Cancel)

21. (Currently amended) The conjugate according to claim 1 ~~any one of the preceding claims~~, wherein linker 3 provides a spacer of a length of 1-25 atoms, preferably a length of 6-18 atoms, or groups of atoms.

22-25. (Cancel)

26. (Original) The conjugate according to any one of the preceding claims, wherein it is



wherein n is 2-4, o is 1-6, p is 1-6, R<sub>1</sub> is H, and R<sub>2</sub> is -COOH, and wherein n preferably is 3, o preferably is 3, and p preferably is 3, bound to a cytotoxic agent via the cytotoxic agent binding moiety.

27. (Currently amended) The conjugate according to claim ~~any one of claims 1 –25~~, wherein it is <sup>177</sup>Lu-1033-trastuzumab, i.e. <sup>177</sup>Lu-3-(13'-thioureabenzyl-DOTA)trioxadiazine-1-(13"-biotin-Asp-OH) trioxadiazine-5-isothiocyanato-aminoisophtalate-trastuzumab; <sup>90</sup>Y-1033-trastuzumab; <sup>111</sup>In-1033-trastuzumab; 1033-trastuzumab, wherein thioureabenzyl-DOTA has been replaced with maytansinoid; and 1033-trastuzumab, wherein thioureabenzyl-DOTA has been replaced with doxorubicin.

28. (Currently amended) A medical composition, wherein it comprises the conjugate according to ~~any one of claims 1-27~~ claim 1 together with a pharmaceutically acceptable excipient.

29. (Cancel)

30. (Currently amended) A kit for extracorporeal removal of or at least reduction of the concentration of a non-tissue bound medical composition as defined in ~~any one of claims~~ claim 28 ~~and 29~~, comprising a conjugate according to ~~any one of claims~~ claim 1-26, in the plasma or

whole blood of a mammalian host, wherein said medical composition has previously been introduced in the body of said mammalian host and kept therein a certain time in order to be concentrated to the specific tissues or cells by being attached thereto, said kit comprising

- a) said medical composition, and
- b) an extracorporeal device comprising an immobilized receptor onto which the affinity ligand of the conjugate adheres.

31. (Original) The kit according to claim 30, wherein it comprises antibodies and antigens/haptens or protein and cofactors as affinity ligand/immobilized receptor combinations, preferably biotin or biotin derivatives as affinity ligands and avidin or streptavidin as the immobilized receptor.

32. (Original) The kit according to claim 30, wherein the affinity ligand is absent in the conjugate of the medical composition, and the immobilized receptor is molecularly imprinted polymers interacting with the conjugate.

33. (Currently amended) A method for the treatment of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to ~~any one of claims~~ claim 28 ~~and 29~~ is administered to the mammal in need thereof.

34. (Original) The method according to claim 33, wherein said cancer is breast or ovarian cancer.

35-37. (Cancel)

38. (Currently amended) A method for diagnosing cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to ~~any one of claims~~ claim 28 ~~and 29~~ is administered to the mammalian host.

39. (Original) The method according to claim 38, wherein said cancer is breast or ovarian cancer.

40-41. (Cancel)

42. (Currently amended) A method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to ~~claims claim 28 and 29~~ containing  $^{111}\text{In}$  in a dose of 50-200 MBq/m<sup>2</sup> body surface, preferably 100-150 MBq/m<sup>2</sup> body surface, and a medical composition according to ~~claims claim 28 and 29~~ containing  $^{90}\text{Y}$  as a cytotoxic agent in a dose of 10-20 MBq/kg body weight, preferably 11-15 MBq/kg body weight, are administered to the mammalian host.

43. (Currently amended) A method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to ~~claims claim 28 and 29~~ containing  $^{111}\text{In}$  in a dose of 100-150 MBq/m<sup>2</sup> body surface, and a medical composition according to ~~claims claim 28 and 29~~ containing  $^{90}\text{Y}$  as the cytotoxic agent in a dose of more than >20 MBq/kg body weight, are administered to the mammalian host, either in sequence in said order by a time interval of 6-8 days or simultaneously.

44. (Currently amended) A method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to ~~claims claim 28 and 29~~ containing  $^{177}\text{Lu}$  as the cytotoxic agent in a single dose of 555-2220 MBq/m<sup>2</sup> body surface, preferably 1000-2000 MBq/m<sup>2</sup> body surface, is administered to the mammalian host.

45. (Currently amended) A method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to ~~claims claim 28 and 29~~ containing  $^{177}\text{Lu}$  as the cytotoxic agent in a single dose of more than 2220 MBq/m<sup>2</sup> body surface is administered to the mammalian host together with means to reconstitute the bone marrow or by reduction of the radiation effect on the bone marrow.